

CLAIMS

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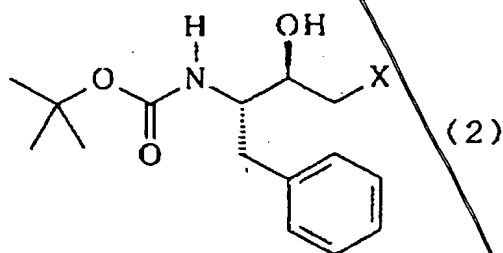
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Sub β 1 25. (Added) A purification/isolation method of a (2R,3S)-1-halo-2-hydroxy-3-N-(tert-butoxycarbonyl)amino-4-phenylbutane of the following general formula (2):



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wherein X represents a halogen atom

which comprises, for the purpose of removing contaminant impurity from a mixture containing (2R,3S)-1-halo-2-hydroxy-3-N-(tert-butoxycarbonyl)amino-4-phenylbutane (2),

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causing the (compound (2)) to be crystallized in the presence of an aliphatic hydrocarbon solvent and collecting the obtained crystals.

26. (Added) The purification/isolation method according

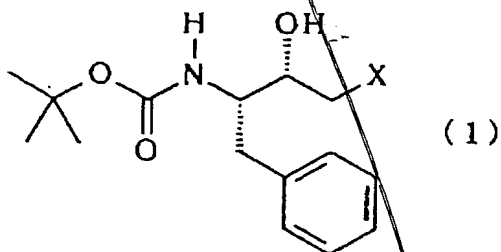
to Claim 25

wherein an aromatic hydrocarbon solvent is used
concomitantly as an auxiliary solvent.

Sub A1 5 27. (Added) The purification/isolation method
according to Claim 26 or 27
wherein the aliphatic hydrocarbon solvent accounts for not
less than 1/2 of the total solvent volume at completion of
crystallization.

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28. (Added) The purification/isolation method
according to Claim 25, 26 or 27
which comprises
causing a compound (1) represented by the following
15 general formula (1):



to be crystallized from a mixture containing said compound (1)
and compound (2) in the presence of an aromatic hydrocarbon
20 solvent as the dominant solvent and collecting the crystals,
and then causing said compound (2) to be crystallized by
substituting an aliphatic hydrocarbon solvent for the dominant
solvent of the mother liquor predominantly having the residual
compound (2)

25 and collecting the obtained crystals.

29. (Added) A purification/isolation method of a
compound (1) and a compound (2)
which comprises

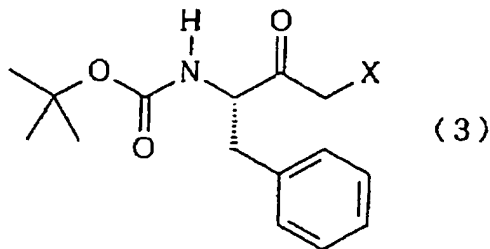
causing said compound (1) to be crystallized from a mixture containing the compound (1) and the compound (2) in the presence of an aromatic hydrocarbon solvent as the dominant solvent and collecting the crystals,

5 and then causing said compound (2) to be crystallized by substituting an aliphatic hydrocarbon solvent for the dominant solvent of the mother liquor predominantly having the residual compound (2).

Sub A¹²
30. (Added) The purification/isolation method according to Claim 28 or 29 wherein an aliphatic hydrocarbon solvent is used concomitantly as an auxiliary solvent at crystallization of the compound (1).

15 31. (Added) The purification/isolation method according to Claim 25, 26, 27, 28, 29 or 30 wherein the crystallization is carried out at a temperature not exceeding 60 °C.

20 32. (Added) The purification/isolation method according to Claim 25, 26, 27, 28, 29, 30 or 31 wherein a mixture containing the compound (2) is obtainable by diastereo-selective reduction of a (3S)-1-halo-2-oxo-3-N-(tert-butoxycarbonyl)amino-4-phenylbutane of the following general formula (3):



wherein X represents a halogen atom.

33. (Added) The purification/isolation method according to Claim 32

wherein the diastereo-selective reduction is carried out
 5 either by using sodium bis(2-methoxy-ethoxy)aluminum hydride,
 lithium aluminum hydride, sodium borohydride, potassium
 borohydride, tetramethylammonium borohydride, an aluminum
 trialkoxide, a lithium aluminum trialkoxy halide or a
 substituted aluminum alkoxide as a reducing agent or by using
 10 a strain of microorganism belonging to the genus Candida,
Geotrichum, Metchnikowia, Pachysolen, Pichia, Rhodotorula,
Trichosporon, or Botryosascus.

34. (Added) The purification/isolation method
 15 according to Claim 32

wherein the diastereo-selective reduction is carried out
 by using a strain of microorganism belonging to the genus
Candida, Pichia, Ogataea, Cryptococcus, Citeromyces,
Debaryomyces, Williopsis, Kloeckera, Lipomyces,
 20 Rhodosporidium, Rhodotorula, Saccharomycopsis or Wingea.

Sub-A3 35. (Added) The purification/isolation method
 according to Claim 32, 33 or 34

wherein the mixture containing the compound (2) is
 25 obtainable by

subjecting the compound (3) to diastereo-selective
 reduction,

extracting said compound (2) from the resulting reaction
 mixture into an organic phase in the presence of an organic
 30 solvent and water,

separating said organic phase from the aqueous phase
 and adjusting it to a concentration suitable for
 crystallization.

36. (Added) The purification/isolation method

according to Claim 35

wherein the mixture containing the compound (2) is obtainable by

5 subjecting compound (3) to diastereo-selective reduction,

10 extracting the reaction mixture with a hydrocarbon solvent and concentrating the separated organic phase or extracting the reaction mixture with an organic solvent and finally substituting a hydrocarbon solvent for the solvent of the separated organic phase.

37. (Added) The purification/isolation method according to Claim 36

15 wherein the mixture containing the compound (2) is obtainable by

20 subjecting said compound (3) to reduction, extracting the reaction mixture with an organic solvent and finally substituting an aliphatic hydrocarbon solvent for the solvent of the separated organic phase.

38. (Added) The purification/isolation method according to Claim 37

25 wherein the mixture containing the compound (2) is obtainable by

30 subjecting said compound (3) to reduction, extracting the reaction mixture with an aromatic organic solvent

35 and finally substituting an aliphatic hydrocarbon solvent for the solvent of the separated organic phase.

39. (Added) The purification/isolation method according to Claim 35, 36, 37 or 38

40 wherein the procedure for giving the mixture containing the compound (2) is carried out at a temperature not exceeding 60 °C.

Sub A4

40. (Added) The purification/isolation method according to Claim 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38 or 39

5 wherein the whole procedure for giving the compound (2) as crystals is carried out at a temperature not exceeding 60 °C.

41. (Added) The purification/isolation method according to Claim 30 or 38

10 wherein the aromatic hydrocarbon solvent is at least one member selected from the group consisting of benzene, toluene, xylene and ethylbenzene.

42. (Added) The purification/isolation method according to Claim 41

15 wherein the aromatic hydrocarbon solvent is toluene.

Sub A5

20 43. (Added) The purification/isolation method according to Claim 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39 or 40

wherein the aliphatic hydrocarbon solvent is at least one member selected from the group consisting of pentane, hexane, methylcyclohexane and heptane.

25 44. (Added) The purification/isolation method according to Claim 43

wherein the aliphatic hydrocarbon solvent is hexane.

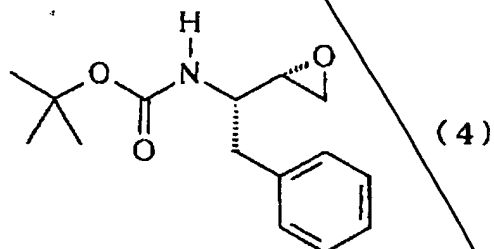
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30 45. (Added) The purification/isolation method according to Claim 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43 or 44

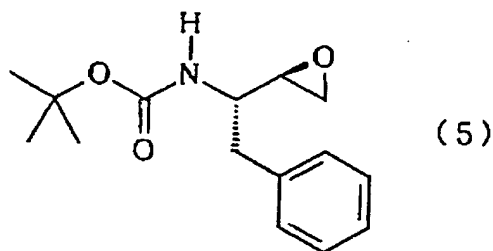
35 wherein the impurity contaminating the mixture containing the compound (2) is at least one member selected from the group consisting of said compound (1), which is the diastereomer, the compound (3), (2S,3S)-1,2-epoxy-3-N-(tert-

Sub A6

butoxycarbonyl) amino-4-phenylbutane of the following general formula (4):



5 and (2R,3S)-1,2-epoxy-3-N-(tert-butoxycarbonyl) amino-4-phenylbutane of the following general formula (5):



10 46. (Added) The purification/isolation method according to Claim 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44 or 45

wherein the halogen atom represented by X in the formula (1), the formula (2) and the formula (3) is chlorine.